BMJ Open

Development of peanut, sesame and tree nut allergy in Polish children at high risk of food allergy: a protocol for a cross-sectional study

Klaudia Ryczaj ,[1] Agnieszka Szczukocka-Zych,[1] Maria Wawszczak,[1] Julia Gawryjołek,[2] Aneta Krogulska,[2] Marta Krawiec,[3,4] Andrea Horvath,[5] Hania Szajewska ,[5] Alexandra Santos,[3,4,6] Henry T Bahnson,[7] Marek Kulus[1]

To cite: Ryczaj K, Szczukocka-Zych A, Wawszczak M, *et al*. Development of peanut, sesame and tree nut allergy in Polish children at high risk of food allergy: a protocol for a cross-sectional study. *BMJ Open* 2023;**13**:e074168. doi:10.1136/bmjopen-2023-074168

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2023-074168).

4 August 2021

KR and MK are joint first authors.

Received 30 March 2023
Accepted 24 October 2023

For numbered affiliations see end of article.

Correspondence to
Klaudia Ryczaj;
klaudia.ryczaj@gmail.com

ABSTRACT

Introduction Peanut allergies cause serious health problems worldwide. A strong finding has shown that the early introduction of peanuts into the diet of infants at high risk of food allergy reduces the prevalence of peanut allergy. Allergies to peanuts, sesame and tree nuts have been shown to coexist in 60% of cases and vary according to geographical location and dietary habits. Insights into the prevalence of nut and seed allergies in societies with varying consumption levels are essential for developing population-specific weaning guidelines. Understanding the age at which peanut allergy develops is paramount for successful early introduction strategies.

Methods and analysis We will perform a cross-sectional study at two tertiary allergy centres in Warsaw and Bydgoszcz. Two hundred forty children aged 4–36 months with eczema or egg allergy will undergo an extensive assessment of their peanut, sesame and tree nut allergy status through skin testing, specific IgE measurements and oral food challenges. The primary outcome is the prevalence of peanut, sesame and tree nut allergies in Polish children at high risk of food allergy. Additionally, the timing of the development of peanut, sesame and tree nut allergies in the first 3 years of life in a high-risk population will be assessed.

Ethics and dissemination The Ethics Committee of the Medical University of Warsaw, Poland approved this protocol (KB/86/2021). The results of this study will be submitted to a peer-reviewed journal no later than 1 year after data collection. The abstract will be presented at relevant national and international conferences. Although the authors may be able to commit to journal submission no later than 1 year after data collection, publication dates remain beyond their control.

Trial registration number NCT05662800.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study will include children aged 4–36 months at high risk of food allergies in Eastern Europe.
⇒ The diagnosis of peanut and sesame allergies will be established based on oral food challenges, the gold standard for food allergy diagnosis.
⇒ The simplified assessment of tree nut allergy will be a limitation in this study.
⇒ Additionally, assessing the timing of food allergy development in a cross-sectional study is another limitation.

INTRODUCTION

Peanut allergy (PA) has been a global health concern for decades. There are several hypotheses for this phenomenon, including different methods of processing peanuts and a delay in the oral introduction of peanuts into children's diets in countries with a high prevalence of PA.[1] Although less prevalent, sesame allergy is a growing concern.[2] PA, sesame and tree nut allergies coexist in 60% of children.[3] Although most PA cases originate in the general population, there are well-established risk factors for this allergy, such as eczema and egg allergy or sensitisation.[4 5] Children aged 4–11 months with egg allergy and moderate-to-severe eczema had a 17% risk of PA in the peanut avoidance group of the Learning Early About Peanut (LEAP) Study.[6] An even higher risk of PA was observed in the HealthNuts Study, where children with early moderate-to-severe eczema and egg allergies had a 35% risk of PA.[7]

In the LEAP Study,[6] the early introduction of peanuts into children's diets with moderate-to-severe eczema or egg allergy was proven effective in PA prevention. This strategy has now been adopted by national allergy societies in North America, the UK and Australia as part of weaning guidance for high-risk populations.[8–10] The European Academy of Allergy and Clinical Immunology prevention guidelines suggest introducing peanuts into infant diets early in populations with a high prevalence of PA.[11] However, it is not known whether peanuts' early introduction

is justified in other populations where peanut consumption has traditionally been lower.[12 13] A recent study from Australia showed the efficacy of early cashew introduction as a means of preventing cashew allergy, suggesting that there may be room for early dietary interventions using tree nuts as a means of preventing food allergies.[14] Obtaining insights into the prevalence of PA, sesame and tree nut allergies in a cohort of infants and toddlers in Eastern Europe is necessary to guide early dietary intervention strategies.

Pooled data from Enquiring About Tolerance (EAT), LEAP and Peanut Allergy Studies suggest that 60% of PA cases develop before the age of 12 months.[15] A few major prospective studies have addressed the timing of food allergy development in the context of its prevention either through early dietary interventions (eg, LEAP, EAT, Prevention of egg allergy in high-risk infants with eczema, Beating Egg Allergy, Hen's Egg Allergy Prevention Studies)[6 16–19] or eczema management (eg, Barrier Enhancement for Eczema Prevention Study, Study of the Atopic March).[20 21] The development of food allergies in these studies was monitored using sensitisation testing throughout the observation period. The confirmation of food allergy with a food challenge, the gold standard of food allergy diagnosis, happened only at the end of some studies at the age of 1–5 years.[22] There are limitations to assessing food allergies using the skin prick test (SPT) and determining specific IgE (sIgE) levels. Data confirming the timing of the development of food allergies in the first years of life through food challenges are lacking. Understanding when food allergies develop early in life is paramount for formulating infant feeding guidelines and adapting preventive policies.

METHODS AND ANALYSIS

This study was designed according to the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline for cross-sectional studies.[23]

Study objective

This study aims to use consumption history, diagnostic tests (SPT and sIgE levels) and oral food challenge (OFC) to assess the prevalence of peanut, sesame and tree nut (hazelnut, almond, cashew, pistachio, walnut and macadamia) allergies in Polish children at a high risk of food allergy. Additionally, the timing of peanut, sesame and tree nut allergies in the first 3 years of life in a high-risk population will be assessed.

Study design

This cross-sectional study will be conducted in Poland in two tertiary allergy centres: Department of Pediatric Pneumonology and Allergy, Medical University of Warsaw, and Department of Pediatrics, Allergology and Gastroenterology, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland.

All eligible participants will undergo diagnostic testing for peanut, sesame and tree nut allergy. To gain a deeper understanding of the risk factors for food allergies and atopic dermatitis endotypes, several subprojects will be conducted. In particular, the roles of the skin barrier, food allergen exposure and serological biomarkers will be investigated. In addition, caregivers' awareness of the early introduction of peanuts into the diet as a means of preventing PA will be assessed. The methods used for these subprojects will be described elsewhere.

Study settings and recruitment

The study will assess allergies to peanuts, sesame and tree nuts in children aged 4 months–3 years with moderate or severe eczema and/or egg allergy. A feasibility assessment of the recruitment capacity of the two centres revealed that a group of 240±10% children can be enrolled over a 2-year period, with 160 participants in Warsaw and 80 participants in Bydgoszcz. The children will be recruited by mail to general paediatric, allergy and dermatology practices, and directly to two allergy centres (Warsaw and Bydgoszcz). Only information regarding the inclusion criteria and invitations to participate in food allergy diagnostics will be made available. Recruitment started on 17 April 2023, and should be completed over 24 months.

Eligibility criteria

Inclusion criteria

At enrolment, the volunteer children were required to fulfil all of the following eligibility criteria to be considered for inclusion: (1) age 4 months–3 years (36 months) (regardless of race, ethnicity or sex); (2) moderate or severe eczema and/or egg allergy; (3) at least one complementary food already introduced; and (4) signed informed consent.

Assessment of eczema severity

Eczema severity will be assessed by trained study physicians based on the objective SCORing Atopic Dermatitis (SCORAD) criteria,[24] use of topical steroids and calcineurin inhibitors, systemic treatment and history of hospital admission (table 1).

Definition of egg allergy

Participants with a documented IgE-mediated egg allergy will be identified by a convincing history of a reaction in the presence of a positive SPT (weal diameter of 3 mm or greater with egg white extract) or an SPT ≥5 mm with no history of a reaction.[25 26]

Exclusion criteria

The exclusion criteria are as follows: inability to discontinue antihistamines for at least 5 days prior to testing, use of prohibited medications such as beta-blockers and ACE inhibitors, and biological treatments affecting the immunological response, uncontrolled asthma, or eczema, which does not guarantee readiness for a food challenge within the study period, and chronic urticaria and/or chronic systemic diseases.

Table 1 Eczema severity assessment

Outgrown or NA	Mild	Moderate	Severe
SCORAD 0 No history of eczema No eczema lesions in the last 6 months	SCORAD 1–15 Topical treatments needed not more than twice in the last 6 months No hospital admissions due to eczema in the last year No systemic treatment for eczema, such as antibiotics, steroids, anti-inflammatory agents, biologicals	SCORAD >15–40 Topical treatments needed every month No hospital admissions due to eczema in the last year No systemic treatment for eczema, such as antibiotics, acyclovir, steroids, anti-inflammatory agents, biologicals	SCORAD >40 Topical treatment needed every month with a recurrent need for moderate or strong topical steroids Hospital admission due to eczema in the last year Need for systemic treatment for eczema in the last year (at least one course of oral antibiotic or acyclovir, systemic steroid, or treatment with anti-inflammatory agents or biologicals)

The table provides guidance only. The final assessment is at the investigator's discretion.
NA, not applicable; SCORAD, SCORing Atopic Dermatitis.

Assessment of asthma control

Asthma control was assessed based on the Global Initiative for Asthma, Global Strategies for Asthma Management and Prevention.[27]

Procedure descriptions

Peanut, sesame and tree nut allergies were assessed based on the history of consumption, diagnostic test results and the OFC.

History of consumption

Parents will be given a questionnaire about their child's consumption of peanuts, sesame and tree nuts with the help of a trained dietitian. The questionnaire was based on a validated questionnaire used in the EAT.[28] Whether the patient consumes the age-appropriate portion (AAP) of a potential food allergen will be determined. Based on the literature, the AAP will be 3 g of protein for peanuts, sesame and tree nuts.[29] Additional information about the history of any reactions after peanut, sesame and tree nut consumption will be collected during the medical history.

Skin prick testing

Children will undergo skin prick testing with the following allergens: commercial extracts of peanut, hazelnut, almond, pistachio, walnut, sesame, Timothy grass and birch pollen; positive and negative controls: peanut butter, tahini (sesame) paste, and fresh cashew and macadamia.

sIgE testing

sIgE levels will be quantified for peanuts, sesame, all the above-listed tree nuts and peanut components (Ara h 1, Ara h 2, Ara h 3, Ara h 6, Ara h 8 and Ara h 9) using ImmunoCAP (Thermo Scientific, Uppsala, Sweden).

Oral food challenges

Peanut and sesame

Children with no convincing allergic reactions to peanuts or sesame who consume an AAP of peanut or sesame protein at least once a month with a negative SPT will be classified as non-allergic (tolerant) without an OFC. Participants meeting predefined criteria based on a history of the presence or absence of an allergic reaction, level of sensitisation and the presence of the allergen in the diet will undertake OFC with peanut AND/OR sesame unless the grade of reaction was severe (classified as 'allergic'). In the case of a low risk of an allergic reaction, for example, in children with a negative SPT without a history of an allergic reaction, a cumulative (single-dose) OFC will be performed. In children at a higher risk of an allergic reaction, for example, children with a history of an allergic reaction but a negative SPT or no history of an allergic reaction but a positive SPT, we will proceed to an incremental OFC (figures 1 and 2).

Tree nut

In terms of tree nuts, patients will be classified as allergic, non-allergic or sensitised depending on the SPT and sIgE results and history of consumption (table 2).

Children with a history of a reaction to a tree nut with a negative SPT and blood test results will undergo an incremental OFC.

Study procedures and timeline

A pre-visit call will occur at least a few days prior to the baseline visit. Information about the child's age, eczema, egg allergy and other common allergic comorbidities, as well as whether at least one complementary food has been introduced into the diet, will be obtained. Information regarding the necessary washout period for antihistamines and beta-mimetics will be provided. Parents will be advised to bring some food preferred by the child and toys to entertain the child. General information will be provided about the planned diagnostic testing for food allergies, without specific information about what foods will be used in the food challenge test.

At the baseline visit, parents will be asked to complete a Nut Consumption Questionnaire during a face-to-face meeting with the help of a trained dietitian. All children with eczema will be diagnosed based on the Hanifin

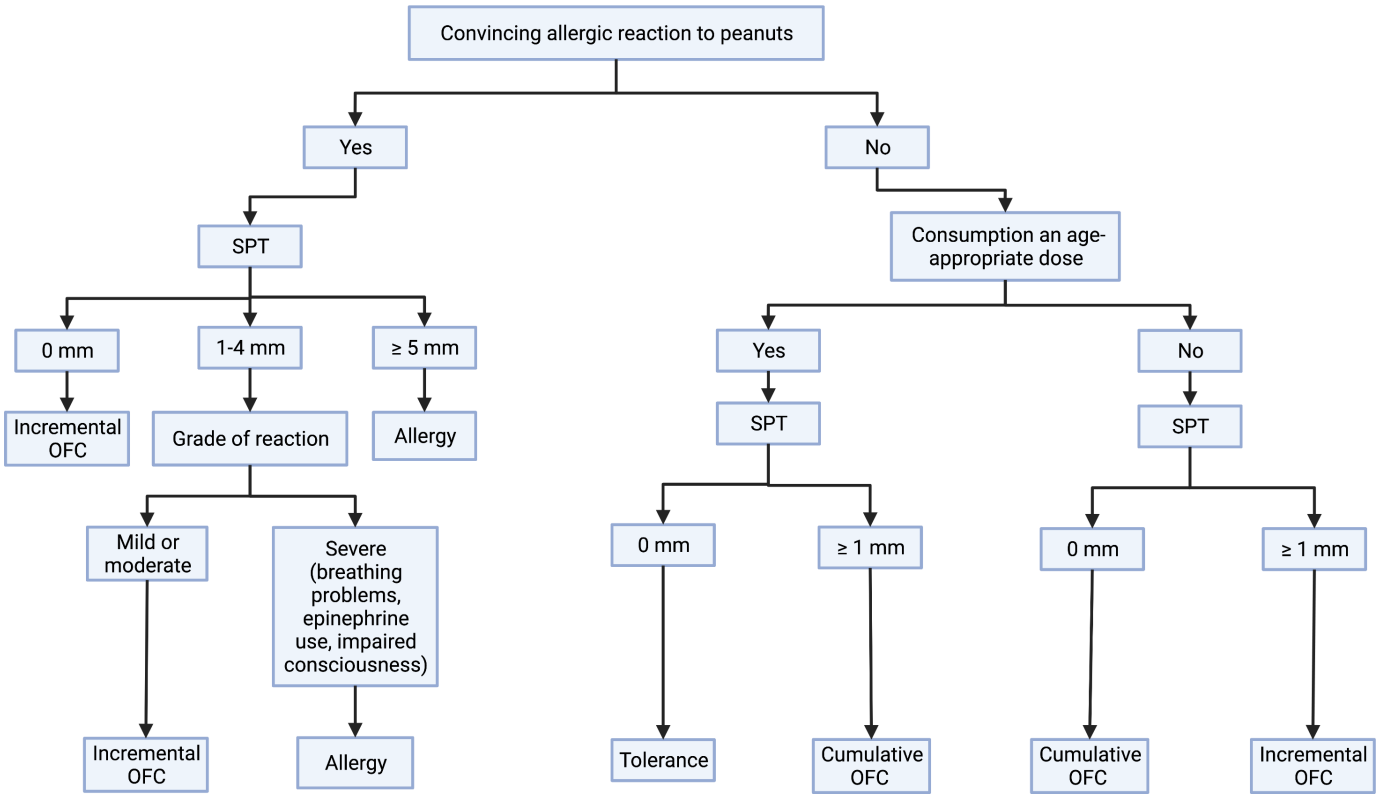

Figure 1 Scheme of oral food challenge (OFC) with peanut. Children with a negative skin prick test (SPT) result for peanuts who eat a predefined age-appropriate portion (AAP) of peanut protein at least once a month will be classified as non-allergic without a food challenge. Children with a negative SPT for peanuts who do not eat an AAP of peanut protein at least once a month will undergo a single-portion peanut challenge with 3.43 g of peanut protein. Children with a positive SPT for peanuts who eat an AAP of peanut protein at least once a month without a history of allergic reactions will undergo a single-portion peanut challenge with an equivalent of 3.43 g of peanut protein. Children with a peanut SPT of 1–4 mm who do not eat peanuts or have a history of mild or moderate reactions will undertake an incremental food challenge. Children with a peanut SPT ≥5 mm who have never eaten peanuts and have not reacted to it in any form will undertake an incremental peanut challenge. Children with a peanut SPT ≥5 mm with a convincing history of reaction to peanuts will not undertake a peanut challenge and will be classified as allergic. Children with a peanut SPT of 0 mm and a history of reaction will undergo an incremental peanut challenge. Children with a positive SPT for peanuts and a well-documented history of severe reactions to peanuts (use of epinephrine, difficulties in breathing, significant behaviour change) will not undertake a food challenge and will be classified as allergic.

and Rajka diagnostic criteria,[30] and the SCORAD will be assessed by trained physicians. All parents will receive oral and written information regarding the study. Parents will be educated about the principles of the study design as well as the risks and benefits.

Children will undergo the SPT performed on the forearm with the following allergens: commercial extracts of peanut, sesame, hazelnut, almond, pistachio, walnut, Timothy grass, birch pollen, positive and negative controls: peanut butter and tahini (sesame) paste. If the tests cannot be performed on the skin of the forearms, the back may be used. If it is not possible to perform all of the scheduled SPT, tests for peanut, sesame and controls will be performed first, followed by tests for tree nuts and then aeroallergens. The study staff performing the SPT will be trained before delegation to the study team. SPTs will be performed in accordance with European guidelines.[31] The reading will be recorded as the longest diameter of the weal at 15 min. The positive and negative control tests will be repeated if the saline negative control test is ≥3 mm or the histamine positive control is ≤3 mm. If the repeat test remains ≥3 mm, the testing should be rescheduled in approximately 7 days.

A 1 mL/kg (max 8 mL) blood sample will be collected by qualified staff from each participant with concomitant insertion of intravenous access in patients qualified for OFC with increasing doses. The serum will be stored at −20°C until further analysis. The determination of sIgE values will be performed at the laboratory in Warsaw.

The decision on whether and which OFC to perform will be based on the largest weal diameter of the peanut tests (peanut extract or peanut butter) and sesame tests (sesame extract or tahini) and presence of allergens in the diet, and the history of presence or absence of an allergic reaction (figures 1 and 2). Only one incremental challenge could occur on a given day. Single-dose challenges can occur on the same day, divided by a minimum of a 1-hour observation period. Peanuts will be the food of choice for the first challenge if more than one challenge is planned.

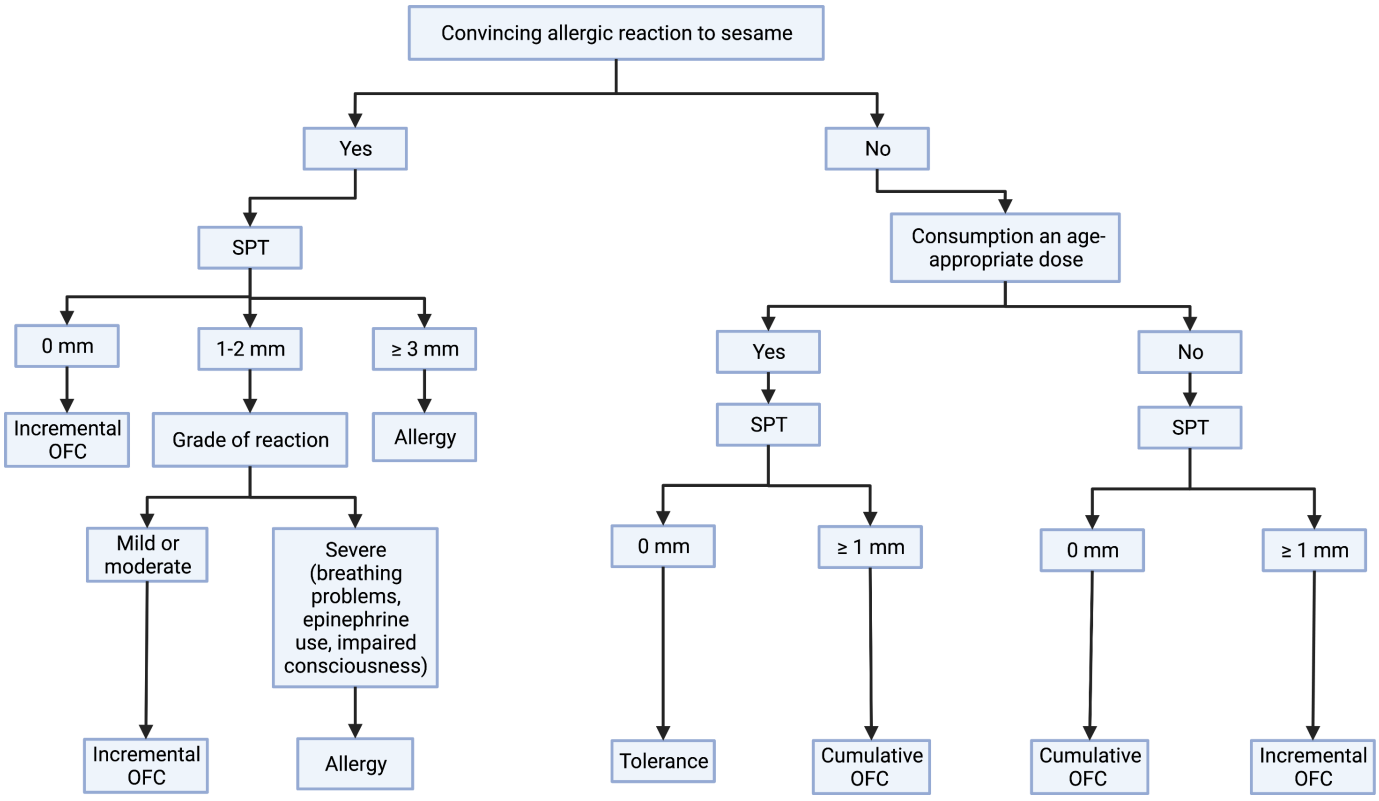

Figure 2 Scheme of oral food challenge (OFC) with sesame. A similar approach to OFC with peanuts will be used, with a cut-off for high-risk challenges of 3 mm. SPT, skin prick test.

Staff members experienced in the procedure will facilitate all OFCs after obtaining additional informed consent from a parent. OFCs will be performed in a hospital setting with immediate access to emergency medical equipment and drugs. Before each dose and 30 min after the completion of the challenge, a short physical examination, including oropharynx inspection, auscultation of the lungs and skin visualisation, will be performed, and the patient's basic vital signs will be measured (blood pressure, pulse and oxygen saturation). In the OFC, with increasing challenges, five sequential doses of food (online supplemental table E1) will be given at intervals 15–20 min. When induced by a single cumulative dose, the dose can be consumed for up to 6 hours. The OFC dosing protocol has been based on the PRACTALL guidelines[32] but modified as in the ProNuts Study.[33] The products that

Table 2 Diagnosis of tree nut allergy

SPT	sIgE	Consumption	Allergy status
Negative	Negative	Eating AAP	Not allergic
Negative	Negative	Eating <AAP or not eating	Indeterminate, likely not allergic
Negative	Negative	Convincing history of reaction	OFC
Positive	Negative	Eating AAP	Not allergic
Positive	Negative	Eating <AAP or not eating	Indeterminate
Positive	Negative	Convincing history of reaction	Allergic
Negative	Positive	Eating AAP	Not allergic
Negative	Positive	Eating <AAP or not eating	Indeterminate
Negative	Positive	Convincing history of reaction	Allergic
Positive	Positive	Eating AAP	Not allergic
Positive	Positive	Convincing history of reaction	Allergic
Positive	Positive	Eating <AAP or not eating	Indeterminate

SPT positive: SPT ≥3 mm; sIgE positive: ≥0.35 kU/L.
AAP, age-appropriate portion; OFC, oral food challenge; sIgE, specific IgE; SPT, skin prick test.

parents can choose from for challenges will be peanut butter or peanut powder and tahini. These products will be administered alone or in combination with products preferred by the child. The PRACTALL OFC guidelines for the indications for discontinuing OFCs will be used. To be considered positive, symptoms should occur within 2 hours of completion of the challenge test. The definition of a positive food challenge will follow the criteria recommended in the PRACTALL guidelines for OFC. To determine the severity score for allergic symptoms during the OFCs, the Modification of the 2010 World Allergy Organization Systemic Allergic Reaction Grading System will be used.[34] We will consider the provocation inconclusive if the patient does not take the cumulative dose and/or if the parent withdraws consent during the OFCs. In the absence of symptoms after challenge with increasing doses, the patient should be observed for at least 2 hours after the last dose or a minimum of 1 hour after provocation with a single cumulative dose. If the clinical history indicates that allergic symptoms occurred later, a longer observation period may be necessary. If a patient develops significant clinical symptoms, up to 4 hours of observation may be required before discharge. If a patient develops a severe systemic allergic reaction requiring significant treatment, then the patient should remain under observation in the hospital overnight.[32]

A follow-up visit will be arranged for the following circumstances: children requiring more than one incremental challenge, patients with a history of tree nut reaction and negative SPT and sIgE results, or if all study procedures were not completed during the baseline visit.

Whenever a patient is enrolled, a case report form (CRF) will be created. Both the CRF and one copy of the informed consent in paper form will be archived. The data from the CRF will be entered into an electronic database.

Concomitant care

A detailed medical history will be obtained from all parents of the patients, and, if necessary, additional appropriate allergy or paediatric diagnostic tests will be performed. Parents of children with eczema should be educated on proper skin care and treatment. Families of patients with a negative peanut and sesame challenge test will be advised to administer an age-appropriate peanut product containing 2 g of peanut or sesame protein (eg, two tablespoons of peanut butter or tahini) at least one time per week, optimally three times per week.[22 35 36] As shown in LEAP and Persistence of Oral Tolerance to Peanuts (LEAP-On) Studies, early peanut introduction and maintenance of this amount in the diet may prevent the development of PA.[6 37] Based on the observed protective benefits of peanuts, it appears reasonable to maintain a diet containing similar quantities of sesame.[36] If feasible, clinical data from patients with negative peanut and/or sesame challenge tests who are encouraged to continue regular consumption of peanuts and/or sesame will be collected prospectively as an independent study. This independent study would examine outcome variables such as eczema exacerbation, subsequent development of PA and/or sesame allergy, food protein-induced enterocolitis, compliance with the advice and reasons for discontinuing the regular consumption of food containing peanuts and/or sesame.

If the challenge test result is positive, the patient's family will be educated on managing an anaphylactic reaction.

Criteria for discontinuing the study procedures

Withdrawal of informed consent will be possible at any time without any obligation for the caregiver to provide reasons for the decision.

Data and participant monitoring

The study will be conducted according to the protocol registered prior to the start of the screening. However, if unexpected and important circumstances arise, the protocol registry will be updated immediately, and if required, the Bioethics Committee will be informed. An independent Data and Safety Monitoring Board will be appointed prior to the study commencement to evaluate each reported adverse event. The Data and Safety Monitoring Board will review the data after recruiting 25%, 50% and 75% of the participants to review all reported adverse events. The number of recruited children will be monitored and kept up to date.

Each caregiver will receive oral and written information regarding the collection and processing of personal data during and after the child's participation in the trial.

Outcomes

The primary outcome of this study will be the prevalence of peanut, sesame and tree nut allergies in Polish children with a high risk of food allergy. Based on the data related to allergen consumption, SPT and OFC in the scheme outlined below (figures 1 and 2), patients will be classified as allergic to peanuts and sesame or non-allergic. Based on the results of the SPT, sIgE and OFCs performed in exceptional situations, according to the classification outlined below (table 2), patients will be classified as allergic, non-allergic or likely not allergic to the selected tree nuts.

Additionally, the timing of the development of peanut, sesame and tree nut allergies in the first 3 years of life in a high-risk population will be assessed.

Sample size

Based on feasibility, 240 children aged 4 months–3 years will be enrolled between the two study centres. To ensure equal representation of children across the investigated age groups, the study will aim to recruit 20% of children aged 4–6 months, 15% aged 7–9 months, 15% aged 10–12 months, 15% aged 13–18 months, 15% aged 19–24 months and 20% in their third year of life.

Statistical analysis

We hypothesised that the prevalence of PA would not exceed 5% at 6 months of age and would reach 20% at

2 years of age. Given the planned sample size based on feasibility, we anticipate a CI for the test in trend detection of the proportion of children with allergies across ages to be adequately powdered with statistically significant precision. Specifically, using a logistic regression model, we estimated the CI width to be approximately 10% across the age range sampled. The model will fit each allergy independently and the cumulative number of allergies using an ordinal logistic regression model, with the age at allergy development as the key independent variable. The power of this test for trend detection is estimated to be greater than 90%. The sampling will be approximately equal across the ages under study, with higher sampling rates at the ends of the age distribution to provide more statistical leverage and, therefore, power to estimate this trend.

Patient and public involvement

None.

Ethics and dissemination

Research ethics approval

This protocol and the informed consent form were approved by the Ethics Committee of the Medical University of Warsaw (approval number: KB/86/2021).

Protocol amendments

Any modification to this version of the protocol that may affect the study design, sample size, research procedures, and/or participant benefit or harm will require a formal protocol amendment. Any modification must be approved by the Ethics Committee of the Warsaw Medical University prior to implementation.

Consent or assent

All caregivers of study participants will provide written informed consent to participate in the study. The MD investigator will have a discussion with the child's caregiver and answer any questions about the study. Included in the main study consent form will be additional consent for collected and partially stored blood samples for future analysis.

Confidentiality

Each participant will have a participant identification number to maintain confidentiality. The electronic database and all electronic records will be password protected and/or stored in password-protected folders.

Access to data

Access to paper and electronic study records will be limited only to the researchers involved in this trial (KR, MW, AS-Z, JG, AH, MK). An external independent statistician will receive access to de-identified electronic dataset.

Ancillary and post-trial care

The compensation of harms will be covered by study insurance policies.

Dissemination policy: trial results

The results of this study will be presented in a peer-reviewed journal no later than 1 year after data collection. The abstract will be presented at relevant national and international conferences.

Author affiliations
[1]Department of Paediatric Pneumonology and Allergy, Medical University of Warsaw, Warsaw, Poland
[2]Department of Paediatrics, Allergy and Gastroenterology, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Bydgoszcz, Poland
[3]Children's Allergy Service, Evelina London Children's Hospital, Guy's and St Thomas' Hospital, London, UK
[4]Department of Women and Children's Health (Pediatric Allergy), School of Life Course Sciences, Faculty of Life Sciences and Medicine, King's College London, London, UK
[5]Department of Paediatrics, Medical University of Warsaw, Warsaw, Poland
[6]Peter Gorer Department of Immunobiology, School of Immunology and Microbial Sciences, King's College London, London, UK
[7]Benaroya Research Institute and the Immune Tolerance Network, Seattle, Washington, USA

Acknowledgements We thank Professor Gideon Lack for his contribution to the study design.

Contributors Conception and design—KR, AS-Z, MKr, AS, HTB and MKu. Writing (original draft)—KR, AS-Z, MKr and HTB. Writing (review and editing)—KR, AS-Z, MW, JG, AK, AH, HS, AS, HTB and MKu. KR, AS-Z, MW, JG, AK, AH, HS, AS, HTB and MKu contributed to and approved the final manuscript. MKu is the guarantor.

Funding This work was supported by NUTRICIA Foundation (grant number RG 2/2021). In addition, Thermo Scientific covered the cost of ImmunoCAP reagents used in the study (no award/grant number).

Competing interests HS has participated as a clinical investigator, and/or advisory board member, and/or consultant, and/or speaker for: Danone, Nestlé/Nestlé Nutrition Institute and Reckitt/Mead Johnson.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Klaudia Ryczaj http://orcid.org/0000-0002-3037-6944
Hania Szajewska http://orcid.org/0000-0002-4596-2874

REFERENCES

1 Platts-Mills TAE. The allergy epidemics: 1870-2010. *J Allergy Clin Immunol* 2015;136:3–13.
2 FDA. Voluntary disclosure of sesame as an Allergen: guidance for industry. 2020. Available: https://www.fda.gov/media/143521/download [Accessed 15 Nov 2022].

3 Brough HA, Caubet J-C, Mazon A, *et al*. Defining challenge-proven coexistent nut and sesame seed allergy: a prospective multicenter European study. *J Allergy Clin Immunol* 2020;145:1231–9.
4 Fleischer DM, Chan ES, Venter C, *et al*. A consensus approach to the primary prevention of food allergy through nutrition: guidance from the American Academy of allergy, asthma, and Immunology. *J Allergy Clin Immunol Pract* 2021;9:22–43.
5 Kotsapas C, Nicolaou N, Haider S, *et al*. Early-life predictors and risk factors of peanut allergy, and its association with asthma in later-life: population-based birth cohort study. *Clin Exp Allergy* 2022;52:646–57.
6 Du Toit G, Roberts G, Sayre PH, *et al*. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med* 2015;372:803–13.
7 Koplin JJ, Peters RL, Dharmage SC, *et al*. Understanding the feasibility and implications of implementing early peanut introduction for prevention of peanut allergy. *J Allergy Clin Immunol* 2016;138:1131–41.
8 Togias A, Cooper SF, Acebal ML, *et al*. Addendum guidelines for the prevention of peanut allergy in the United States: report of the National Institute of allergy and infectious diseases–sponsored expert panel. World Allergy Organ J 2017;10:1.
9 ASCIA Guidelines Infant Feeding and Allergy Prevention 2020, Available: https://www.allergy.org.au/hp/papers/infant-feeding-and-allergy-prevention [Accessed 20 Mar 2023].
10 Stiefel G, Anagnostou K, Boyle RJ, *et al*. BSACI guideline for the diagnosis and management of peanut and tree nut allergy. *Clin Exp Allergy* 2017;47:719–39.
11 Halken S, Muraro A, de Silva D, *et al*. EAACI guideline: preventing the development of food allergy in infants and young children (2020 update). *Pediatr Allergy Immunol* 2021;32:843–58.
12 Prusak A, Schlegel-Zawadzka M, *et al*. Consumer perceptions of peanuts and peanut allergy: the Europrevall results of focus groups in Poland. *Public Health Open J* 2017;2:11–20.
13 Prusak A, Schlegel-Zawadzka M, Boulay A, *et al*. Characteristics of the peanut chain in Europe - implications for peanut allergy. *Acta Sci Pol Technol Aliment* 2014;13:321–33.
14 Peters RL, Barret DY, Soriano VX, *et al*. No cashew allergy in infants introduced to cashew by age 1 year. *J Allergy Clin Immunol* 2021;147:383–4.
15 Roberts G, Bahnson HT, Du Toit G, *et al*. Defining the window of opportunity and target populations to prevent peanut allergy. *J Allergy Clin Immunol* 2023;151:1329–36.
16 Perkin MR, Logan K, Tseng A, *et al*. Randomized trial of introduction of allergenic foods in breast-fed infants. *N Engl J Med* 2016;374:1733–43.
17 Natsume O, Kabashima S, Nakazato J, *et al*. Two-step egg introduction for prevention of egg allergy in high-risk infants with Eczema (PETIT): a randomised, double-blind, placebo-controlled trial. *The Lancet* 2017;389:276–86.
18 Wei-Liang Tan J, Valerio C, Barnes EH, *et al*. A randomized trial of egg introduction from 4 months of age in infants at risk for egg allergy. *J Allergy Clin Immunol* 2017;139:1621–8.
19 Bellach J, Schwarz V, Ahrens B, *et al*. Randomized placebo-controlled trial of hen's egg consumption for primary prevention in infants. *J Allergy Clin Immunol* 2017;139:1591–9.
20 Chalmers JR, Haines RH, Bradshaw LE, *et al*. Daily Emollient during infancy for prevention of Eczema: the BEEP randomised controlled trial. *The Lancet* 2020;395:962–72.
21 Spergel JM, Boguniewicz M, Schneider L, *et al*. Food allergy in infants with atopic dermatitis: limitations of food-specific IGE measurements. *Pediatrics* 2015;136:e1530–8.
22 Krawiec M, Fisher HR, Du Toit G, *et al*. Overview of oral tolerance induction for prevention of food allergy—where are we now *Allergy* 2021;76:2684–98.
23 Vandenbroucke JP, von Elm E, Altman DG, *et al*. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *Epidemiology* 2007;18:805–35.
24 Kunz B, Oranje AP, Labrèze L, *et al*. Clinical validation and guidelines for the SCORAD index: consensus report of the European task force on Atopic dermatitis. *Dermatology* 1997;195:10–9.
25 Hill DJ, Heine RG, Hosking CS. The diagnostic value of skin prick testing in children with food allergy. *Pediatr Allergy Immunol* 2004;15:435–41.
26 Du Toit G, Roberts G, Sayre PH, *et al*. Identifying infants at high risk of peanut allergy: the learning early about peanut allergy (LEAP) screening study. *J Allergy Clin Immunol* 2013;131:135–43.
27 Global Initiative for Asthma. Global strategy for asthma management and prevention. 2022. Available: https://www.ginasthma.org [Accessed 15 Nov 2022].
28 Perkin MR, Logan K, Marrs T, *et al*. Enquiring about tolerance (EAT) study: feasibility of an early Allergenic food introduction regimen. *J Allergy Clin Immunol* 2016;137:1477–86.
29 Bird JA, Leonard S, Groetch M, *et al*. Conducting an oral food challenge: an update to the 2009 adverse reactions to foods committee work group report. *J Allergy Clin Immunol Pract* 2020;8:75–90.
30 Hanifin JM, Rajka G. Diagnostic features of Atopic dermatitis. *Acta Derm Venereol* 1980;60:44–7.
31 Bousquet J, Heinzerling L, Bachert C, *et al*. Practical guide to skin prick tests in allergy to Aeroallergens. *Allergy* 2012;67:18–24.
32 Sampson HA, Wijk R, Bindslev-Jensen C, *et al*. Standardizing double-blind, placebo-controlled oral food challenges: American Academy of allergy:: *J Allergy Clin Immunol* 2012;130:1260–74.
33 Brough HA, Caubet J-C, Mazon A, *et al*. Defining challenge-proven coexistent nut and sesame seed allergy: A prospective multicenter European study. *J Allergy Clin Immunol* 2020;145:1231–9.
34 Cox LS, Sanchez-Borges M, Lockey RF. World allergy organization systemic allergic reaction grading system: is a modification needed *The Journal of Allergy and Clinical Immunology: In Practice* 2017;5:58–62.
35 Bird JA, Groetch M, Allen KJ, *et al*. Conducting an oral food challenge to peanut in an infant. *J Allergy Clin Immunol Pract* 2017;5:301–11.
36 Fisher HR, Lack G, Roberts G, *et al*. Medical algorithm: early introduction of food Allergens in high-risk populations. *Allergy* 2021;76:1592–4.
37 Du Toit G, Sayre PH, Roberts G, *et al*. Effect of avoidance on peanut allergy after early peanut consumption. *N Engl J Med* 2016;374:1435–43.